The Egyptian Journal of Hospital Medicine (October 2024) Vol. 97, Page 3977-3985

Role of Target Artery Revascularization of a Specific Angiosome for Limb Salvage in Patients with Chronic Limb-Threatening Ischemia

Mohamed AbdelSamie Abdelkhalek Elbahat*
Vascular and Endovascular Department, Shebin Elkoom Teaching Hospital,
General Organisation for Teaching Hospitals and Institutes, Egypt
*** Corresponding author:** Mohamed AbdelSamie Abdelkhalek Elbahat,
Email: mohamedelbahat_2010@yahoo.com, **Phone:** +2 01003923421

ABSTRACT
Background: Chronic limb-threatening ischemia (CLTI) patients often experience severe complications that can lead to amputation. Advances in revascularization techniques aim to improve patient outcomes, however the efficacy of direct versus indirect approaches remains under evaluation.
Objectives: This study aimed to compare direct and indirect revascularization techniques in CLTI patients and to assess outcomes over a 12-month follow-up period. The study also considered angiosome-based ulcer classification, demographic factors, and atherosclerosis risk factors.
Patients and methods: A prospective cohort of 46 CLTI patients was divided into two equal groups based on the revascularization technique: Direct (n=23) and indirect (n=23). Clinical outcomes assessed included amputation-free survival, major adverse limb events (MALE), and wound healing rates.
Results: The direct group had a significantly higher amputation-free survival rate (91.3%) compared to the indirect group (69.6%, p=0.03). Freedom from MALE was also higher in the direct group (87% vs. 56.5%, p=0.02), as was the major amputation-free rate (91.3% vs. 73.9%, p=0.05). Wound healing rates were notably better in the direct group (82.6% vs. 52.2%, p=0.02). Kaplan-Meier analysis highlighted superior survival curves for amputation-free survival, MALE, and major amputation rates in the direct group.
Conclusion: Direct revascularization techniques offer superior outcomes in amputation-free survival, MALE, and wound healing for CLTI patients compared to indirect techniques.
Keywords: Amputation-free survival, Critical limb ischemia, Direct revascularization, Indirect revascularization, Major adverse limb events.

INTRODUCTION

Over the past 15 years, studies have explored how revascularization via endovascular procedures or surgical bypass guided by the angiosome concept (AC), can enhance foot vascular mapping for individuals with chronic limb-threatening ischemia (CLTI) [1]. The Global Vascular Guidelines (GVG) now favor the term CLTI over "critical" or "severe" limb ischemia, as the latter terms are tied to specific hemodynamic thresholds that do not encompass the full range of contributing factors related to high amputation rates and reduced long-term survival [2].

CLTI manifests primarily as a form of peripheral artery disease, with patients experiencing persistent rest pain or developing diabetic foot ulcers (DFUs) that persist beyond two weeks. This severe condition represents a major burden on healthcare systems, frequently resulting in hospital stay and limb amputation, whereas substantially diminishing patients' quality of life and rising medical expenses [3].

The condition carries significant cardiovascular risks and poor survival outcomes, with more than 30% of cases progressing to major amputation and a concerning one-year mortality rate of 25% [4]. The condition is marked by low awareness, delayed diagnosis, and variability in medical practices, leading to diverse treatment outcomes [5].

Type 2 diabetes significantly increases CLTI risk, with studies indicating that one in four diabetic patients will develop an ulcer, and 85% of major amputations in diabetics are preceded by ulcers, 65% of which are ischemic [6]. The Society for Vascular Surgery has implemented the WIf I classification system to assess lower limb risks in managing CLTI, evaluating wound severity, ischemia, and infection to guide CLTI nical decisions. As wound complexity and infection severity rise, the need for revascularization becomes more urgent [7].

The angiosome concept, first introduced by Taylor and Palmer in 1987, segments the body into three-dimensional regions supplied by specific source arteries, demonstrating their role in providing blood to various tissues [6, 7]. Studies expanded this concept by identifying six angiosomes in cadaver legs, revealing three angiosomes on the plantar foot, two on the ankle and hindfoot, and one on the dorsum, all supplied by distinct arteries [8, 9].

This study's objective was comparing the direct outcomes versus indirect revascularization techniques in CLTI patients over a 12-month follow-up period,

Received: 06/06/2024
Accepted: 07/08/2024

considering angiosome-based ulcer classification and the impact of demographic and atherosclerosis risk factors.

PATIENTS AND METHODS

This study involved CLTI patients owing to isolated below-the-knee (BTK) lesions who underwent successful revascularization via endovascular therapy (EVT), defined as achieving flow through at least one vessel to the pedal arch without bypass surgery. All patients had confirmed ankle arch distal flow prior to the procedure. This study recruited 46 consecutive patients with CLTI characterized by non-healing ulcers, gangrene, or both (Rutherford stages 5 or 6), stemming from isolated BTK lesions. The participants were split into two groups: The direct group, comprising 23 patients with restored blood flow to the ulceration site through EVT, and the indirect group, consisting of 23 patients without successful flow restoration. For wounds spanning multiple territories, all relevant arteries were treated, categorizing these patients in the direct group.

CLTI nical history and examination were conducted for all patients, documenting age, gender, and major atherosclerosis risk factors comprising diabetes, smoking, hypertension, and ischemic heart disease. Preoperative vascular assessments included evaluating arterial pulsations, measuring the ankle-brachial index (ABI), and recording tissue loss extent. Routine laboratory tests, comprising complete blood count and kidney function, were performed alongside vascular assessments using Duplex scans and CT angiography in 40% of cases.

Vascular surgeons assessed EVT indications for each patient, who were fully informed about the procedure, risks, benefits, and alternatives before providing consent. EVT was indicated for lesions with ≥ 50% diameter stenosis affecting a non-healing ulcer or gangrene. Patients were admitted before or on the procedure day, with a 300 mg loading dose of clopidogrel administered the night prior. EVT was performed under local anesthesia, with intravenous antibiotics given as necessary. The ipsilateral common femoral artery (CFA) was the preferred access route using a 6F sheath, with 5000 IU of unfractionated heparin administered after sheath insertion.

During the procedure, digital subtraction angiography confirmed the nonhealing ulceration location and angiosome-based target lesion. An angiosome-based intervention was attempted; if successful, other lesions with residual stenosis were not treated. If the angiosome-based intervention failed, non-angiosome-based lesions were addressed. The foot was categorized into six angiosomes based on arterial supply (Figure 1).

Angiosomes		**Branches**	**Feeders**
Dorsum of the foot	①Red	Dorsalis Pedis a. (and Anterior Perforator of PA)	ATA
Lateral ankle	②Orange	Lateral Calcaneal a.	PA
Planter heel	③Green	Lateral Calcaneal a. (and Calcaneal Branch of PTA)	
Medial ankle	④Light Blue	Calcaneal Branch	PTA
Medial instep	⑤Blue	Medial Plantar a.	
Lateral~plantar forefoot	⑥Yellow	Lateral Plantar a.	

Figure 1: The angiosomes in the foot and its feeders [10] .

The posterior tibial artery (PTA) supplies the medial aspect of the rear foot and the entire plantar surface of the foot, encompassing three angiosomes. The peroneal artery (PA) is responsible for supplying blood to the lateral ankle and the plantar heel. Meanwhile, the anterior tibial artery (ATA) provides blood to a single area.

The antegrade approach was preferred, utilizing a 6F sheath. If unsuccessful, retrograde tibiopedal access was employed. For long tibial occlusions, stiff 0.018 wires were used first, followed by 0.035 wires if necessary. Balloons of 2.5 to 3 mm in diameter and slightly longer than the lesion were utilized for dilatation, with inflation pressure and time adjusted based on the balloon type. Stents were reserved for complicated cases.

Success was defined by CLTI clinical improvements (e.g., regained pulse, warmth, reduced edema) and angiographic success as < 30% residual stenosis at the narrowest lumen point. In isolated peroneal artery cases, success was determined by good distal collateralization.

Post-procedural management involved immediate sheath removal, with digital compression at the puncture site. Mobilization was delayed for 12-24 hours, especially after significant heparin administration. Most patients received discharge on the second day, along with instructions for risk factor management and medications to take, including low molecular weight heparin, aspirin, clopidogrel, and antihyperlipidemic drugs as needed.

Patients received foot care, including wound dressing and infection control before discharge. Follow-up occurred monthly, assessing pulse, ulcer healing, infection resolution, and study outcomes, primarily focusing on amputation-free survival (AFS), freedom from major adverse limb events (MALE), and major amputation rates, aligning with international standards for evaluating catheter-based therapies in CLTI.

Ethical considerations: The study was conducted following approval from the Research Ethics Committee of the Vascular and Endovascular Department at Shebin Elkoom Teaching Hospital. Written informed consents were obtained from all patients prior to their enrollment. The consent form detailed their agreement to participate in the study and to the publication of anonymized data, ensuring confidentiality and privacy. The study adhered to the ethical principles outlined in the Declaration of Helsinki by the World Medical Association for research involving human participants.

Statistical analysis

Statistical analysis was carried out utilizing SPSS software version 28.0 (IBM Corp., Armonk, NY, USA), with data distribution normality estimated through the Shapiro-Wilk test. For continuous variables showing normal distribution, results were presented as mean ± SD, whereas categorical data were shown as frequencies and percentages. Comparisons among groups employed independent samples t-tests for normally distributed continuous variables, and either Chi-square or Fisher's exact tests for categorical data. The study utilized Kaplan-Meier curves and log-rank testing for evaluating survival outcomes, comprising amputation-free survival, MALE, and major amputation rates. For determining predictors of major amputation, multivariate Cox regression analysis was done, generating hazard ratios (HRs) with 95% confidence intervals (CIs). Statistical significance was established at $p \leq 0.05$.

RESULTS

The study encompassed 46 participants, with an average age of 62.5 years. Males encompassed 67.4% of the cohort, with similar distributions across direct (63.5 years) and indirect (61.5 years) groups. Average diabetes duration was 14.3 years, and mean HbA1c was 7.3%, with no significant differences across groups. Hypertension affected 69.6%, and 45.7% were smokers. Other comorbidities, comprising coronary artery disease (34.8%) and dyslipidemia (52.2%), revealed no significant variation across groups (Table 1).

Table (1): Patient characteristics (demographics and comorbidities)

Variable	Overall (n=46)	Direct (n=23)	Indirect (n=23)	p-value
Patient demographics				
Age (Years)	62.5 ± 11.8	63.5 ± 10.5	61.5 ± 12.7	0.60
Gender				0.78
- Male	31 (67.4%)	16 (69.6%)	15 (65.2%)	
- Female	15 (32.6%)	7 (30.4%)	8 (34.8%)	
Comorbidities				
Duration of DM	14.3 ± 6.5 years	14.7 ± 6.3	13.9 ± 6.8	0.70
HbA1c (%)	7.3 ± 1.5	7.5 ± 1.3	7.2 ± 1.6	0.45
Hypertension	32 (69.6%)	16 (69.6%)	16 (69.6%)	1.00
Smoking	21 (45.7%)	11 (47.8%)	10 (43.5%)	0.78
Coronary Artery Disease (CAD)	16 (34.8%)	9 (39.1%)	7 (30.4%)	0.53
Dyslipidemia	24 (52.2%)	12 (52.2%)	12 (52.2%)	1.00
End-Stage Renal Disease (ESRD)	4 (8.7%)	2 (8.7%)	2 (8.7%)	1.00
Hemodialysis	3 (6.5%)	1 (4.3%)	2 (8.7%)	0.55
Stroke	8 (17.4%)	4 (17.4%)	4 (17.4%)	1.00
Heart Failure	11 (23.9%)	6 (26.1%)	5 (21.7%)	0.73
Atrial Fibrillation	5 (10.9%)	2 (8.7%)	3 (13%)	0.63
Myocardial Infarction	6 (13%)	3 (13%)	3 (13%)	1.00

SD: Standard Deviation, DM: Diabetes Mellitus, HbA1c: Hemoglobin A1c, CAD: Coronary Artery Disease, ESRD: End-Stage Renal Disease.

The largest proportion of patients fell into Rutherford class 5 (56.5%) or class 6 (43.5%), with no significant differences observed across the groups (p = 0.55). The affected arteries distribution and lesion locations revealed no significant differences across the groups (p = 0.78 for artery involvement; p = 0.90 for lesion location). Pre-procedure ABI was similar (p = 0.60), and mean affected angiosomes was 2.2 overall, with no significant differences observed across the groups (p = 0.30) (Table 2).

Table 2: Lower limb and lesion characteristics

Variable	Overall (n=46)	Direct (n=23)	Indirect (n=23)	p-value
Rutherford classification				
- Rutherford 5	26 (56.5%)	14 (60.9%)	12 (52.2%)	0.55
- Rutherford 6	20 (43.5%)	9 (39.1%)	11 (47.8%)	
Affected arteries (below the knee)				
- Anterior Tibial Artery (ATA)	16 (34.8%)	9 (39.1%)	7 (30.4%)	0.78
- Posterior Tibial Artery (PTA)	13 (28.3%)	7 (30.4%)	6 (26.1%)	
- Peroneal Artery (PA)	11 (23.9%)	5 (21.7%)	6 (26.1%)	
- Dorsalis Pedis artery	6 (13%)	2 (8.8%)	4 (17.4%)	
Location of ulcers/gangrene				
- Toes	17 (36.9%)	9 (39.2%)	8 (34.8%)	0.90
- Heel	12 (26.1%)	7 (30.4%)	5 (21.7%)	
- Dorsum of Foot	9 (19.6%)	4 (17.4%)	5 (21.7%)	
- Plantar of Foot	5 (10.9%)	2 (8.7%)	3 (13%)	
- Ankle	3 (6.5%)	1 (4.3%)	2 (8.8%)	
ABI (pre-procedure)	0.70 ± 0.23	0.72 ± 0.22	0.68 ± 0.24	0.60
ABI (post-procedure)	0.86 ± 0.21	0.89 ± 0.19	0.83 ± 0.22	0.40
Number of Angiosomes Affected	2.2 ± 0.8	2.0 ± 0.7	2.4 ± 0.9	0.30

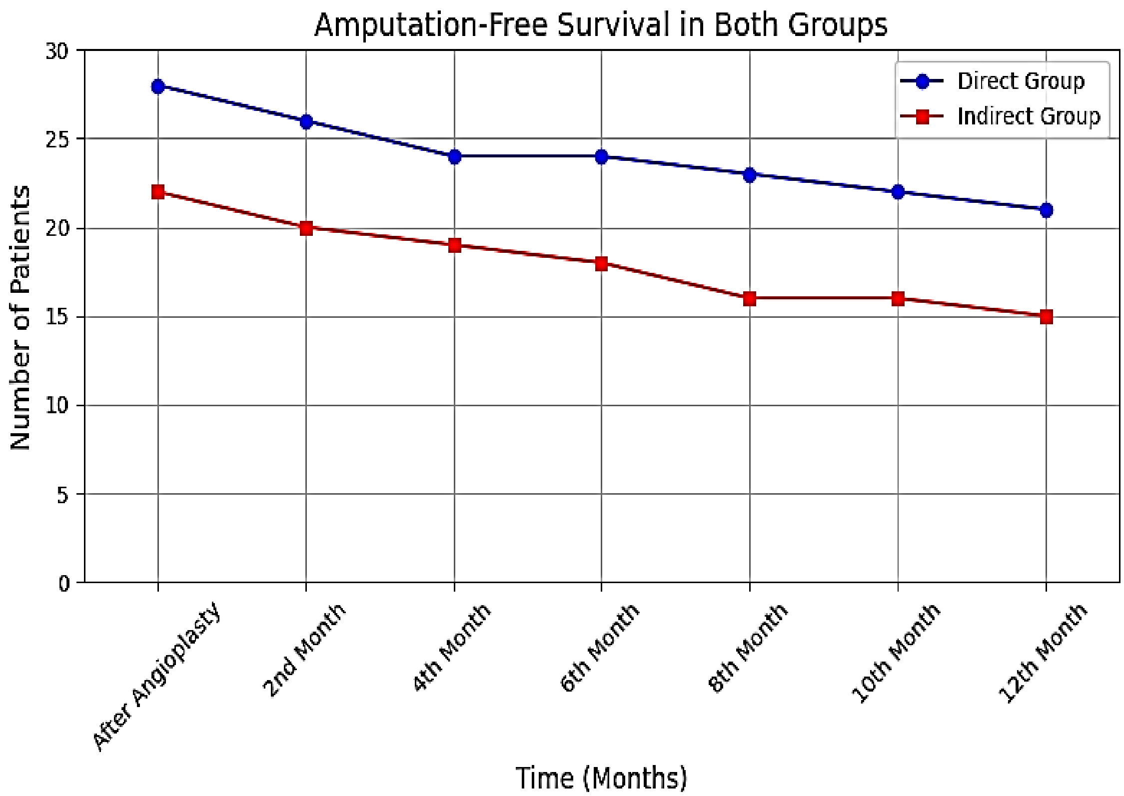
ATA: Anterior Tibial Artery, PTA: Posterior Tibial Artery, PA: Peroneal Artery, ABI: Ankle-Brachial Index.

Most procedures were carried out via the ipsilateral femoral approach (91.3%), with no differences between groups (p = 1.00). Lesions were primarily crossed using a transluminal approach (80.4%). In 8.7% of the cases, minor complications occurred, with no major complications reported (Table 3).

Table 3: Procedural data

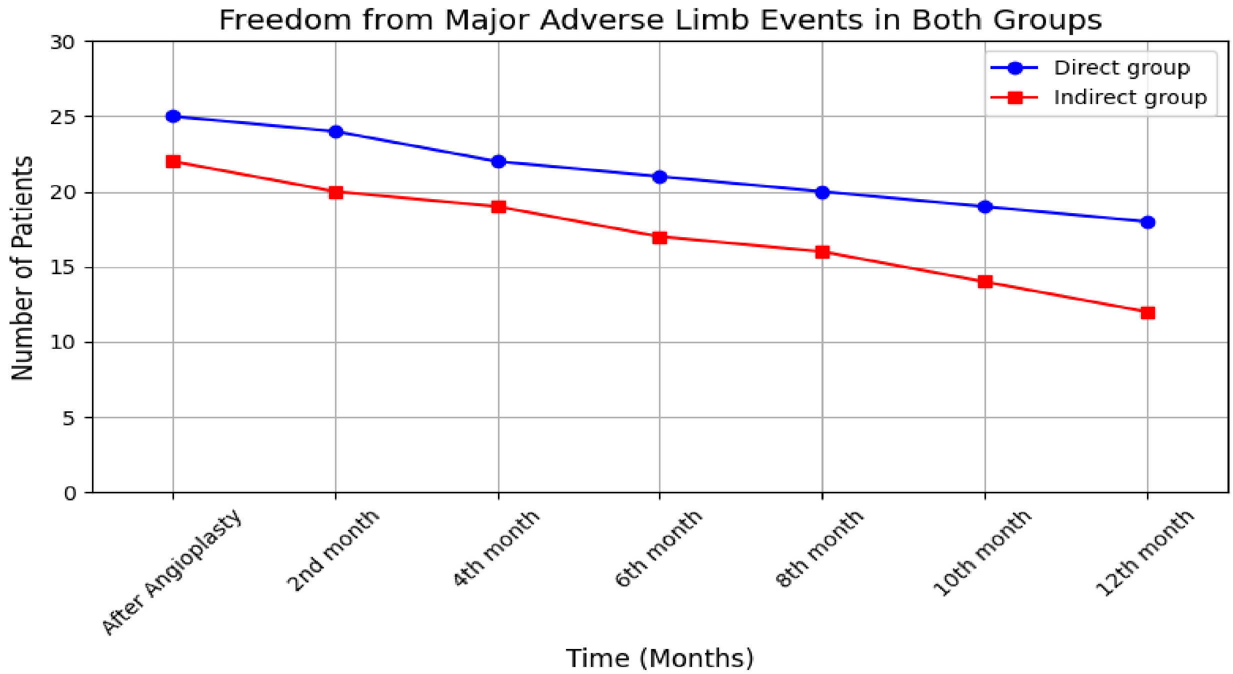
Variable	Overall (n=46)	Direct (n=23)	Indirect (n=23)	p-value
Access site				
- Ipsilateral Femoral Approach	42 (91.3%)	21 (91.3%)	21 (91.3%)	1.00
- Contralateral Approach	4 (8.7%)	2 (8.7%)	2 (8.7%)	
Crossing lesion				
- Transluminal Cross	37 (80.4%)	19 (82.6%)	18 (78.3%)	0.71
- Subintimal Cross	9 (19.6%)	4 (17.4%)	5 (21.7%)	
Stenting	0 (0%)	0 (0%)	0 (0%)	-
Minor Complications	4 (8.7%)	2 (8.7%)	2 (8.7%)	1.00
Major Complications	0 (0%)	0 (0%)	0 (0%)	-

At 12 months, amputation-free survival was significantly greater in the direct group (91.3%) in comparison with the indirect group (69.6%) (p = 0.03) (Figure 2). Freedom from major adverse limb events and major amputation rates also favored the direct group (p = 0.02 and p = 0.05 respectively) (Figures 3 & 4).



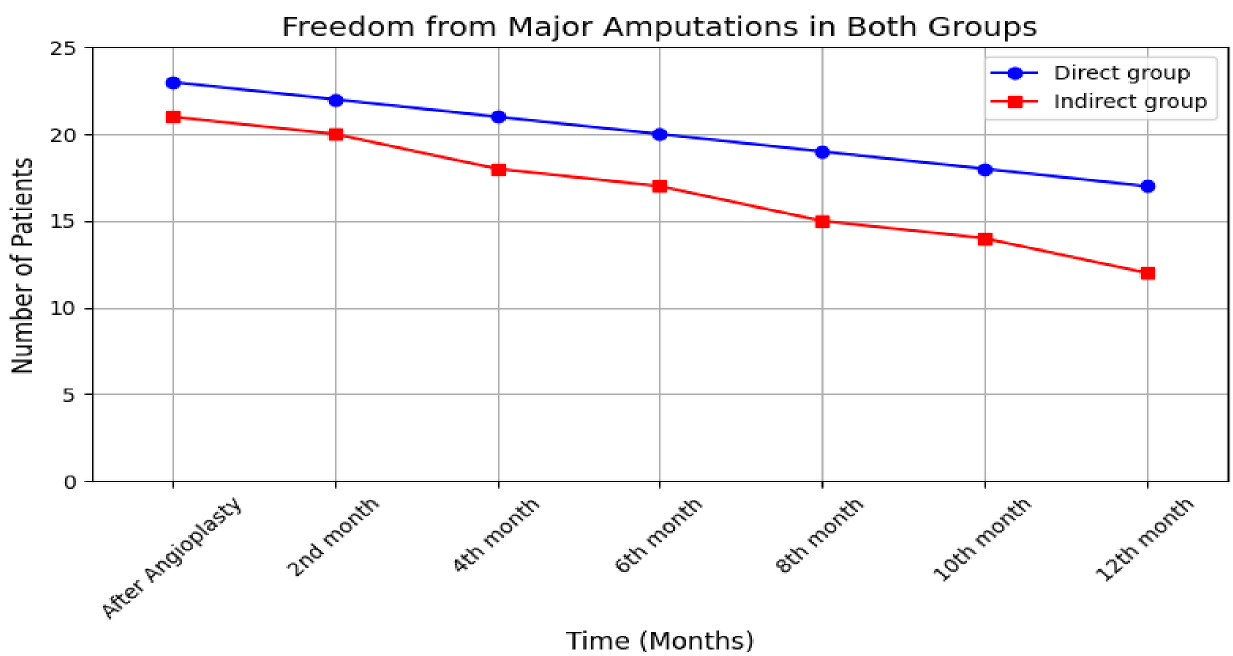
	After Angioplasty	2nd Month	4th Month	6th Month	8th Month	10th Month	12th Month
Direct Group	28	26	24	24	23	22	21
Indirect Group	22	20	19	18	16	16	15

Figure (2): Curves showing amputation-free survival in both groups.



	After Angioplasty	2nd Month	4th Month	6th Month	8th Month	10th Month	12th Month
Direct Group	25	24	22	21	20	19	18
Indirect Group	22	20	19	17	16	14	12

Figure (3): Curves showing freedom from major adverse limb in both groups.



	After Angioplasty	2nd Month	4th Month	6th Month	8th Month	10th Month	12th Month
Direct Group	23	22	21	20	19	18	17
Indirect Group	21	20	18	17	15	14	12

Figure (4): Curves showing freedom from Major Amputations in both groups

The overall wound healing rate was 67.4%, significantly greater in the direct group (82.6%) in comparison with the indirect group (52.2%) (p = 0.02) (Table 4).

Table (4): 12-Month follow-up outcomes

Outcome	Overall (n=46)	Direct (n=23)	Indirect (n=23)	p-value
Amputation-Free Survival (AFS)	37 (80.4%)	21 (91.3%)	16 (69.6%)	0.03*
Freedom from Major Adverse Limb Events (MALE)	33 (71.7%)	20 (87%)	13 (56.5%)	0.02*
Freedom from Major Amputation (MA)	38 (82.6%)	21 (91.3%)	17 (73.9%)	0.05*
Wound Healing Rate	31 (67.4%)	19 (82.6%)	12 (52.2%)	0.02*

AFS: Amputation-Free Survival, MALE: Major Adverse Limb Events, MA: Major Amputation.

Cox proportional hazard analysis indicated that smoking and coronary artery disease were significant predictors of major amputation, with smoking increasing risk by 30% (p = 0.04) and CAD by 35% (p = 0.03). Other factors, comprising age and diabetes duration, were not significant predictors (Table 5).

Table (5): Multivariate Cox proportional hazard analysis (risk of major amputation)

Variable	Hazard Ratio (HR)	95% CI	p-value
Age	1.10	0.85–1.40	0.25
Diabetes Duration (per 5 years)	1.20	0.95–1.55	0.10
Smoking	1.30	1.00–1.70	0.04*
Coronary Artery Disease (CAD)	1.35	1.05–1.75	0.03*
Pre-procedure ABI	0.80	0.55–1.15	0.30
Affected Artery (Anterior Tibial)	0.85	0.65–1.25	0.40

HR: Hazard Ratio, CI: Confidence Interval.

DISCUSSION

The controversy regarding the benefits of angiosome-guided revascularization is substantial, as highlighted by the global vascular guidelines (GVG) [11]. A significant challenge in angiosome-based treatment lies in the accurate classification of foot wounds according to specific angiosomes, which is feasible in only a limited number of cases [12]. This challenge is exemplified in toe lesions, which constitute a substantial portion of cases and typically receive dual blood supply from both the anterior and posterior tibial arteries (ATA and PTA). Another crucial consideration involves the technical feasibility of accessing the target vessel within the intended angiosome territory [13].

These complexities have sparked ongoing discussions in the medical community regarding the relative merits and effectiveness of "direct" versus "indirect" revascularization approaches from both hemodynamic and clinical perspectives [14].

Direct revascularization refers to the technique of restoring blood circulation specifically to the angiosome containing the ulcerated area, whereas indirect revascularization focuses on improving blood flow to a neighbouring, ulcer-free angiosome region. This fundamental difference in approach characterizes these two distinct revascularization strategies [14]. Most existing literature primarily examines these methods through retrospective analyses focused on outcomes like amputation-free survival and wound healing [15, 16]. However, these results can be affected by a variety of factors beyond the specific strategies employed [17].

Wound characteristics can differ greatly, resulting in unique treatment approaches and varying blood flow requirements for optimal healing. The revascularization effectiveness, particularly via direct endovascular techniques, is greatly dependent on the specific stage of the wound [18].

In their study of foot angiosomes, **Ferraresi *et al.*** [19] underscored the essentiality of conducting thorough imaging studies of the vascular network in the leg and foot before deciding on a revascularization strategy. This approach provides a clearer insight into the primary arteries distribution and their spatial relationships, allowing for customized treatment plans that take into account the patient's individual anatomy [20].

As previously indicated, the revascularization main goal in CLTI patients is facilitating wound healing and avoid amputation [21]. Various strategies exist for achieving revascularization. Studies examining CLTI patients who received distal bypass procedures revealed similar wound healing outcomes between those treated with targeted and non-targeted angioplasty approaches when patient characteristics were balanced using propensity score analysis. These results suggest that the angiosome-based approach might be less critical in bypass surgery cases, particularly across individuals without end-stage renal disease. Instead, factors related to the characteristics of ischemic wounds, including their location, extent, and the presence of comorbidities, appear to have a more considerable influence on healing outcomes [22].

Whether using a direct or indirect surgical revascularization method, selecting the most suitable vessel for the procedure is critical. In contrast, endovascular revascularization provides the benefit of precise angiosome targeting, which may be critical for improving patient outcomes. However, this technique can require extensive and complex methods that may not always result in positive outcomes. The bypass surgery endures essentiality, as it has the ability to produce higher local pressure and sustain normal physiological pulsatile blood flow. Moreover, endovascular methods can support the reconstruction of multiple vessels beneath the knee and ankle [23].

A comprehensive investigation executed by **Špillerová and colleagues** (7) examined 580 CLTI patients presenting with foot ulcers or gangrene, wherein 407 patients received endovascular treatment and 173 underwent surgical revascularization of infrapopliteal vessels. Their findings emphasized the angiosome-directed revascularization essentiality, particularly in endovascular thrombectomy (EVT) procedures when the pedal arch was incomplete. The study identified several independent risk factors for poor limb salvage, comprising high C-reactive protein (CRP) values, rheumatoid arthritis, and the compromised angiosomes' number. With these factors having greater impact in cases where pre-operative imaging revealed an incomplete pedal arch. Furthermore, a meta-analysis by **Chae and Shin** (22) demonstrated that angioplasty focused on angiosomes notably improved overall limb salvage rates and outcomes related to wound healing.

The successful treatment of CLTI extends beyond surgical procedures alone, regardless of their effectiveness. Critical aspects of care include comprehensive postoperative management, encompassing both appropriate medication regimens and meticulous wound care protocols. This is especially crucial for patients with comorbid conditions like end-stage renal disease (ESRD) or diabetes, as these conditions can significantly compromise wound healing processes and immune system function.

CONCLUSION

Direct revascularization techniques demonstrated superior outcomes in terms of amputation-free survival, freedom from major adverse limb events, and wound healing compared to indirect techniques in patients with CLTI.

Financial support and sponsorship: Nil.
Conflict of Interest: Nil.

REFERENCES

1. **Chou T, Alvelo J, Janse S *et al.* (2021)**: Prognostic Value of Radiotracer-Based Perfusion Imaging in Critical Limb Ischemia Patients Undergoing Lower Extremity Revascularization. JACC Cardiovasc Imaging, 14: 1614-24.
2. **van den Berg J (2018)**: Angiosome perfusion of the foot: An old theory or a new issue? Semin Vasc Surg., 31: 56-65.
3. **Tay S, Abdulnabi S, Saffaf O *et al.* (2021)**: Comprehensive Assessment of Current Management Strategies for Patients With Diabetes and Chronic Limb-Threatening Ischemia. Clin Diabetes, 39: 358-88.
4. **Palena L, Garcia L, Sultato E *et al.* (2014)**: Angiosomes: how do they affect my treatment? Tech Vasc Interv Radiol., 17: 155-69.
5. **Lejay A, Georg Y, Tartaglia E *et al.* (2014)**: Long-term outcomes of direct and indirect below-the-knee open revascularization based on the angiosome concept in diabetic patients with critical limb ischemia. Ann Vasc Surg., 28: 983-9.
6. **Conte M, Bradbury A, Kolh P *et al.* (2019)**: Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia. Eur J Vasc Endovasc Surg., 58: S1-S109.e33.
7. **Špillerová K, Biancari F, Settembre N *et al.* (2017)**: The Prognostic Significance of Different Definitions for Angiosome-Targeted Lower Limb Revascularization. Ann Vasc Surg., 40: 183-9.
8. **Elsayed S, Clavijo L (2015)**: Critical limb ischemia. Cardiol Clin., 33: 37-47.
9. **Huang T, Huang T, Wang Y *et al.* (2015)**: Direct Revascularization With the Angiosome Concept for Lower Limb Ischemia: A Systematic Review and Meta-Analysis. Medicine (Baltimore), 94: e1427.
10. **Okazaki J, Ishida M, Kuma S *et al.* (2015)**: Infrapopliteal bifurcated dual run-off bypass in critical limb ischemia: a report of 2 cases. Ann Vasc Surg., 29: 1020.e17-21.
11. **Vallabhaneni R, Kalbaugh C, Kouri A *et al.* (2016)**: Current accepted hemodynamic criteria for critical limb ischemia do not accurately stratify patients at high risk for limb loss. J Vasc Surg., 63: 105-12.
12. **Vogel T, Petroski G, Kruse R (2014)**: Functional status of elderly adults before and after interventions for critical limb ischemia. J Vasc Surg., 59: 350-8.
13. **Partridge J, Dhesi J, Cross J *et al.* (2014)**: The prevalence and impact of undiagnosed cognitive impairment in older vascular surgical patients. J Vasc Surg., 60: 1002-11.e3.
14. **Bosanquet D, Glasbey J, Williams I *et al.* (2014)**: Systematic review and meta-analysis of direct versus indirect angiosomal revascularisation of infrapopliteal arteries. Eur J Vasc Endovasc Surg., 48: 88-97.
15. **Uccioli L, Gandini R, Giurato L *et al.* (2010)**: Long-term outcomes of diabetic patients with critical limb ischemia followed in a tertiary referral diabetic foot clinic. Diabetes Care, 33: 977-82.
16. **Sumpio B, Forsythe R, Ziegler K *et al.* (2013)**: Clinical implications of the angiosome model in peripheral vascular disease. J Vasc Surg., 58: 814-26.
17. **Biancari F, Juvonen T (2014)**: Angiosome-targeted lower limb revascularization for ischemic foot wounds: systematic review and meta-analysis. Eur J Vasc Endovasc Surg., 47: 517-22.
18. **Wang C, Yang S, Zhang J *et al.* (2017)**: An Overview of Pre-expanded Perforator Flaps: Part 1, Current Concepts. Clin Plast Surg., 44: 1-11.

19. **Ferraresi R, Centola M, Ferlini M *et al.* (2009)**: Long-term outcomes after angioplasty of isolated, below-the-knee arteries in diabetic patients with critical limb ischaemia. Eur J Vasc Endovasc Surg., 37: 336-42.
20. **Hata Y, Iida O, Mano T (2019)**: Is Angiosome-Guided Endovascular Therapy Worthwhile? Ann Vasc Dis., 12: 315-8.
21. **Orrapin S, Siribumrungwong B (2024)**: Successful Revascularization, Angiosome Concept, and Multivessel Revascularization: Effects on Wound Healing: An Asian Perspective. Int J Low Extrem Wounds, 23: 12-8.
22. **Rueda C, Nehler M, Perry D *et al.* (2008)**: Patterns of artery disease in 450 patients undergoing revascularization for critical limb ischemia: implications for clinical trial design. J Vasc Surg., 47: 995-9.
23. **Kodama A, Meecham L, Popplewell M *et al.* (2020)**: Editor's Choice - Relationship Between Global Limb Anatomic Staging System (GLASS) and Clinical Outcomes Following Revascularisation for Chronic Limb Threatening Ischaemia in the Bypass Versus Angioplasty in Severe Ischaemia of the Leg (BASIL)-1 Trial. Eur J Vasc Endovasc Surg., 60: 687-95.